PB86-224532

Comparison of Plasma Cholinesterase Depression Among Workers Occupationally Exposed to Organophosphorus Pesticides as Reported by Various Studies

Miami Univ., FL

Prepared for

Health Effects Research Lab.
Research Triangle Park, NC

1986

U.S. Department of Commerce
National Technical Information Service
NTIS

TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO. EPA/600/J-86/106	2.
3. R PB86-224532	
4. TITLE AND SUBTITLE (Journal Version) Comparison of Plasma Cholinesterase Depression Among Workers Occupationally Exposed to Organophosphorus Pesticides as Reported by Various Studies	5. REPORT DATE 1986
	6. PERFORMING ORGANIZATION CODE
7. AUTHOR(S) [1]Robert C. Duncan, [2]Jack Griffith, and [1]Janet Konefal	8. PERFORMING ORGANIZATION REPORT NO.
9. PERFORMING ORGANIZATION NAME AND ADDRESS [1]University of Miami School of Medicine Miami, Florida [2]USEPA, HERL,RTP,NC	PROGRAM ELEMENT NO.
	11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Health Effects Research Laboratory - RTP,NC Office of Research and Development U.S. Environmental Protection Agency Research Triangle Park, NC 27711	13. TYPE OF REPORT AND PERIOD COVERED
	14. SPONSORING AGENCY CODE EPA/600/11

15. SUPPLEMENTARY NOTES

REF: Journal of Toxicology and Environmental Health, 18(1):1-11, July 1986

16. ABSTRACT

A number of studies have reported on the inhibitory effects of organophosphorus pesticides (OPs) on the enzyme cholinesterase (ChE) among agricultural workers. With the increasing use of OPs, surveys of blood ChE activity on exposed workers may help to identify workers at greatest risk and to provide insight into the use history--e.g., mixing, loading, application, and harvesting--that might lead to a hazardous situation. Although it does appear that measurements of ChE activity are valuable in worker surveillance programs, it is difficult to interpret findings from various studies since they are dependent on the method of assay and the emphasis is usually placed on statistical tests (i.e., p values) that depend on the number of subjects studied. In the present paper a method is presented to compare ChE values reported in several studies utilizing various methods and units of measurement, and to assess the impact of OP exposure as a percentage of subjects with ChE values depressed below the normal limits.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group

18. DISTRIBUTION STATEMENT RELEASE TO PUBLIC	19. SECURITY CLASS (This Report) UNCLASSIFIED	21. NO. OF PAGES 12
	20. SECURITY CLASS (This page) UNCLASSIFIED	22. PRICE

EPA Form 2220-1 (Rev. 4-77) PREV

REPRODUCED BY NATIONAL TECHNICAL INFORMATION SERVICE U.S. DEPARTMENT OF COMMERCE SPRINGFIELD, VA. 22161

EPA/600/J-86/106
JOURNAL ARTICLE

COMPARISON OF PLASMA CHOLINESTERASE DEPRESSION AMONG WORKERS OCCUPATIONALLY EXPOSED TO ORGANOPHOSPHORUS PESTICIDES AS REPORTED BY VARIOUS STUDIES

Robert C. Duncan

University of Miami School of Medicine, Department of Oncology, Miami, Florida

Jack Griffith

U.S. Environmental Protection Agency, Health Effects Research Laboratory, Research Triangle Park, North Carolina

Janet Konefal

University of Miami School of Medicine, Department of Epidemiology, Miami, Florida

A number of studies have reported on the inhibitory effects of organophosphorus pesticides (OPs) on the enzyme cholinesterase (ChE) among agricultural workers. With the increasing use of OPs, surveys of blood ChE activity on exposed workers may help to identify workers at greatest risk and to provide insight into the use history—e.g., mixing, loading, application, and harvesting—that might lead to a hazardous situation. Although it does appear that measurements of ChE activity are valuable in worker surveillance programs, it is difficult to interpret findings from various studies since they are dependent on the method of assay and the emphasis is usually placed on statistical tests (i.e., p values) that depend on the number of subjects studied. In the present paper a method is presented to compare ChE values reported in several studies utilizing various methods and units of measurement, and to assess the impact of OP exposure as a percentage of subjects with ChE values depressed below normal limits.

INTRODUCTION

A number of studies have reported on the inhibitory effects of organophosphorus pesticides (OPs) on red blood cell cholinesterase

This study was funded by the National Pesticide Hazard Assessment Program, Office of Pesticide Programs, Environmental Protection Agency, Washington, D.C. (CR80705101). The views expressed herein are those of the investigators and do not necessarily reflect the official viewpoint of the funding agency. We are very grateful to Mary Burrus for her excellent work in typing this manuscript. We also want to thank the reviewers for providing helpful suggestions in developing the contents of this paper.

Requests for reprints should be sent to Jack Griffith, U.S. Environmental Protection Agency, Health Effects Research Laboratory (MD-55A), Research Triangle Park, North Carolina 27711.

Journal of Toxicology and Environmental Health, 18:1–11, 1986
Copyright © 1986 by Hemisphere Publishing Corporation

NTIS is authorized to reproduce and sell this report. Permission for further reproduction must be obtained from the copyright owner.

(RBChE) and plasma cholinesterase (PChE) enzymes among agricultural fieldworkers (Tabershaw and Cooper, 1966; Burns and Parker, 1975; Ware et al., 1975; Popendorf et al., 1979; Kraus et al., 1981).

One approach has been to compare differences in group mean values among OP-exposed workers and controls for "statistically significiant" depression among the exposed (Tocci et al., 1969; Levin et al, 1976). It is well known that the finding of statistically significant differences between mean values depends strongly on sample size. Thus, two studies with the same mean difference between exposed and controls might lead to different conclusions. Also, a difference in mean values does not directly address the distribution of individual values.

Another approach has been to compare individual preexposure values to exposure values, and report the findings as a percent of depression experienced by the worker (Burns and Parker, 1975; Wicker et al., 1979). Also, Knaak et al. (1978) and Bodgen et al. (1975), among others, have investigated cholinesterase (ChE) depression in workers complaining of cholinergic symptoms following OP exposure.

Since measurements of blood ChE activity are frequently dependent on the method of assay, and since inter- and intraperson variation may also confound interpretation, they are not always comparable (Gage, 1967). To further make comparability difficult, it is well known that exposed workers often have depressed ChE values compared to controls (Popendorf et al., 1979; Kraus et al., 1981; Levin et al., 1976; Wicker et al., 1979). Therefore, the utilization of ChE measurements may provide little insight into the severity of a pesticide-related incident, and may not permit comparison with findings in other investigations.

Wolfsie and Winter (1952) have suggested that study results derived from different assay methods may be compared by converting the measure of dispersion of a series of experiments to percentage form, using the coefficient of variation. However, the coefficient of variation is concerned with population averages, primarily within a normal range of values (PChE; 15–25%; RBChE; 10–15%), and has limited usefulness in comparing results from various studies. Perhaps a more effective means of comparison would be similar to the approach used by Milby et al. (1964) and Tocci et al. (1969), who expressed the severity of OP exposure experienced by agricultural fieldworkers by determining the percentage of exposed workers with ChE values below normal values provided by an unexposed control population. In order to do this, however, the individual observations are necessary.

The physiology of ChE inhibition as a result of OP exposure has been well described (Durham and Hayes, 1962; Vandekar, 1980) and will not be discussed in detail here, except to say the RBChE has been reported to closely parallel the level of ChE in the central and peripheral parasympathetic nervous system (Vandekar, 1980; Freedman et al.,

1949; Zavon, 1965) and is considered to be the best indicator of acetylcholinesterase activity at the nerve synapse. However, PChE has been called the most sensitive measure of OP exposure (Grob and Harvey, 1949; Bogusz, 1968; Rider et al., 1969) and perhaps provides the best early warning of excessive OP exposure (Levin et al., 1976; Wicker et al., 1979).

In the present paper a method, based on summary statistics, is presented to compare PChE values, reported in several studies utilizing various assay methods and units of measurement, through the use of the dimension-free standardized deviation unit of measurement independent of sample size, and to assess the impact of OP exposure on the various study populations by estimating the percentage of workers with PChE values depressed below the lower limit of normal (one-tailed, 95% confidence limit) compared to unexposed control values. Although the procedure described is as suitable for RBChE as for PChE, for the reasons described above, we decided to use PChE in our demonstration of the standardization method (Δ).

METHODS

The standard deviation unit of measurement (Δ) is obtained by expressing differences between group mean ChE values divided by the pooled standard deviation of the distribution of the values, i.e., in standard deviation units. The greater the arithmetic value of Δ, the greater the estimated exposure to OPs.

In defining the standardized unit of measurement Δ, it is assumed that cholinesterase levels will be depressed. Letting $\bar{X}_C$, $\bar{X}_E$, and SD denote the control mean, the exposed mean, and the pooled standard deviation, respectively, we define $\Delta = (\bar{X}_C - \bar{X}_E)/\text{SD}$. Thus Δ measures the shift in the exposed mean in terms of standard deviation units.

Assuming normality of the distribution of cholinesterase values among subjects, which seems justifiable based on the biochemical/physiological nature of the variable, data reported in the literature, and the relative size of the standard deviations to the means for the various methods, we may define the lower 95% normal limit based on the control mean as $X_L = \bar{X}_C - 1.645\text{SD}$. Thus for any study, we would expect 5% of the control subjects to have values below X_L. That is, X_L is an estimate of the fifth percentile of the distribution of control values.

If an exposed group has its mean value shifted by Δ standard deviation units, while maintaining the same shape for the distribution of values, it can be shown that the expected percent of exposed subjects below the normal limit for their controls is given by $\phi(\Delta - 1.645) \times 100$, where ϕ indicates the area under the standard normal (Z) curve from minus infinity to $\Delta - 1.645$. As an example, let $\Delta = 2.17$ (Study

TABLE 1. A Comparison of Plasma Cholinesterase Depression among Workers Occupationally Exposed to Organophosphorus Pesticide as Reported by Various Studies

Study groups	Unit of measurement	n	$\bar{X}$	SD	p Values[a]	Standard unit of measurement Δ	Lower limit[b] of normal	Percent of exposed workers below normal
[1] Controls	μmol/min/ml	217	4.06	1.04				
[1] Exposed	μmol/min/ml	505	3.80	1.09	0.01	0.24	2.29	7.9
[2] Controls (White)	Δ pH units/h	34	0.94	0.199				
[2] Formulators (White)	Δ pH units/h	25	0.81	0.169	0.01	0.71	0.64	17.9
[3] Preexposed Orchard Workers	Δ pH units/h	14	0.83	0.150[c]				
[3] Exposed Orchard Workers	Δ pH units/h	13	0.74	0.070[c]	nsd	0.82	0.65	20.6
[4] Controls	μ/mil · min	23	4.82	1.47				
[4] Exposed Farmers and PCO's	μ/mil · min	23	3.78	1.01	0.01	0.84	2.77	20.6
[5] Controls	μ/mil · min	24	4.98	1.53				
[5] CA's	μ/mil · min	13	3.48	1.16	0.01	1.11	2.75	29.5
[2] Controls (white)	Δ pH units/h	34	0.94	0.199				
[6] Citrus Fieldworkers	Δ pH units/h	128	0.73	0.157	0.001	1.33	0.68	35.9
[7] Preexposed Cotton Scouts	μmol/mil · min	21	2.80	0.6				
[7] Exposed Cotton Scouts	μmol/mil · min	10	1.90	0.7	0.001	1.38	1.73	39.7
[2] Controls (Black)	Δ pH units/h	15	0.95	0.168				
[2] Formulators (Black)	Δ pH units/h	10	0.74	0.132	0.002	1.40	0.70	39.4
[3] Certified Applicators (pre-exposure)	Δ pH units/h	16	0.91	0.12[c]				
[3] Certified Applicators (exposed)	Δ pH units/h	30	0.67	0.16[c]	0.001	1.60	0.66	47.2
[8] Controls	IU/ml	15	3.70	0.930				
[8] Pesticide Factory Workers	IU/ml	75	1.96	0.673	0.001	2.17	2.38	70.2
[9] Controls	IU/ml	2	7.60	1.13				
[9] Migrant Workers	IU/ml	12	4.30	1.41	0.01	2.60	5.50	82.9
[10] Controls	μmol/min · ml	95	9.40	1.60				
[10] Exposed Grape Pickers	μmol/min · ml	79	3.50	1.30	0.001	4.07	7.01	99.2

[a] Student's t-test.
[b] One-tailed 95% confidence limit.
[c] Derived value.

group 8, Table 1). Then ϕ (2.17 − 1.645) × 100 = ϕ (0.525) × 100 = 70.2. Although not presented in this report, the standard errors for these estimates could be computed using the method, based on the Z statistic, suggested by Callaway et al. (1951). Mean values are compared using the Student's t-test.

RESULTS AND DISCUSSION

Data reported from 10 different studies are summarized in Table 1. The data are grouped for explicit statistical comparisons and demonstrate some redundancy. The order of appearance in the table is based on the increasing numerical value of Δ. The discussions which follow all refer to Table 1, where the reference numbers, within square brackets, are used to index the study giving rise to the data.

[1] Warnick and Carter (1972) reported on a series of clinical and biochemical tests on 505 subjects who were moderately occupationally exposed to pesticides, and compared the results to 217 closely matched controls. The participants were subjects in the Community Pesticide Study (Simmons, 1968) of the U.S. Public Health Service, and represent long-term exposure to OP and other pesticide compounds. The exposed subjects had a statistically significantly ($p < 0.01$) depressed PChE value compared to controls. The Δ (0.24) for the exposed workers is less than 1 SD unit, indicating moderate exposure to OP compounds. Only 7.9% of the exposed workers would be expected to have PChE values below the lower limit (2.29 μmol/min · ml) of normal for the controls. Symptomatically, no effects of clinical significance were observed in the occupationally exposed workers, although among the interesting findings was a significantly ($p < 0.05$) elevated serum creatinine value for the pesticide applicators among the exposed population.

[2] Tocci et al. (1969) compared PChE levels found in the blood of Florida workers formulating OP compounds, with unexposed controls, matched for age and race. The formulators, black and white, had statistically significantly depressed PChE values compared to controls. The Δ (0.71) for the white formulators is less than 1 SD unit, indicating little exposure to OP compounds, while the Δ (1.40) for the black formulators is approaching 1½ SD units and indicates significant exposure to OPs. This interpretation is supported by Tocci et al. (1969), who identified the black formulators as the most exposed group studied. Only 18% of the white formulators would be expected to have PChE values below the lower limit of normal for the controls, while 39% of the black formulators would be expected to have PChE values below the normal limit. Symptomatically, the black formulators experienced serum creatinine levels significantly elevated beyond normal levels when compared to matched controls, while the white formulators did not experi-

ence a similar rise in creatinine levels. Tocci et al. (1969) suggested that the significant elevation in creatinine levels among black formulators reflected pesticide-induced renal dysfunction.

[3] Hayes et al. (1957) tested orchard workers and commercial pesticide applicators in 1952 and 1953, respectively, for depressed PChE levels following exposure to OP compounds (preexposure values for the exposed workers served as controls). The exposed orchard workers experienced a definite, but not statistically significant decrease in PChE levels. The Δ (0.82) for the orchard workers is slightly less than 1 SD and is consistent with increasing OP exposure. Almost 21% of the exposed orchard workers would be expected to have PChE values below the 0.65 Δ pH units/h lower limit of normal for the pre-exposure control values. The orchard workers may have experienced more illness symptomatic of Op intoxication, e.g., headache, nausea, weakness or fatigue, pain or tightness in the chest, sweating, blurred vision, anorexia, and myosis; however, as a result of the design of the 1952 survey, it was impossible to statistically associate these illnesses with the orchard workers. In 1953, adjustments were made in the survey methodology, and, as shown further down in Table 1, preexposure and exposure PChE values are shown for commercial applicators. The difference between the means was statistically significant at the $p < 0.001$ level. The Δ is more than 1½ SD units and suggests significant exposure to OPs. More than 47% of all the commercial applicators would be expected to have PChE values below the 0.66Δ pH units/h lower limit of normal for preexposure values. Symptomatically, the commercial applicators experienced an increase in cholinergic like illnesses during the exposure period. Symptoms of headache, nausea, pain or tightness in the chest, and myosis were most apparent, and led Hayes et al. (1957) to conclude that the occurrence of myosis or three or more selected symptoms suggests the diagnosis of mild OP intoxication.

[4] Rodnitzky et al. (1975), in an attempt to associate chronic but nonacute pesticide exposure with central nervous system dysfunction (Durham and Hayes, 1962), compared a group of 12 farmers and 11 commercial pesticide applicators regularly exposed to OP compounds with a group of matched but unexposed controls. Although it remained in the "normal" range, the mean PChE value for the exposed group was statistically significantly lower than the mean value for the controls. Almost 21% of the exposed group would be expected to have PChE values below the 2.77 μ/mil · min lower limit of normal measurement for the controls. The Δ (0.84) for the exposed group signaled increasing but limited exposure to OPs. No deficiency was noted in the exposed group in relation to memory, signal processing, vigilance, language, or proprioceptive feedback, and no illness was reported at the time of testing.

[5] Levin et al. (1976) compared commercial pesticide applicators

(CAs) with unexposed matched (age, sex, and race) controls to evaluate the frequency of selected psychiatric symptoms in workers chronically but not acutely exposed to OPs. The mean PChE value for the CAs is statistically significantly depressed ($p < 0.01$) when compared to the unexposed controls, and the Δ (1.11) is greater than 1 SD unit, indicating an increasing exposure to OPs. Almost 30% of the CAs would be expected to have PChE values below the 2.75 μ/mil · min lower limit of normal for the controls. Symptomatically, CAs were found to have greater anxiety than controls; however, they did not differ in the frequency of depression, impairment of concentration, and mental confusion.

[6] Griffith and Duncan (1985), in a study described elsewhere, measured PChE among 73 spray season citrus workers and 55 citrus harvesters. The observed PChE mean values are statistically significantly different from the "normal" values used by [2] Tocci et al. (1969) for control values. The Δ for the two citrus groups is about 1.3 SD units, suggesting significant exposure to OPs and leading to an estimation of 36% of citrus workers chronically having PChE values below the lower limit of normal (0.68Δ pH units/h) for the control group. However, in a review of the correlation of cholinergic-like symptoms with urinary OP metabolites, no direct effect of exposure was found (Duncan and Griffith, 1985).

[7] Wicker et al. (1979) observed PChE levels of cotton scouts inspecting foliage for insect infestation and damage, and comparisons were made between preexposure and exposure levels. Although no symptoms of organophosphate poisoning were confirmed among the scouts studied, the observed PChE values were significantly lower than baseline values. The difference between the means was statistically significant at the $p < 0.001$ level. The Δ (1.38) is approaching 1.4 SD units and reflects significant exposure to OP compounds by the cotton scouts. Almost 40% of the exposed workers would be expected to have PChE values below the 1.73 μmol/mil · min lower limit of normal determined by preexposure values.

[8] Bhatnagar et al. (1982) compared PChE values in 75 pesticide factory workers with 15 nonexposed controls. The difference between the means was statistically significant at the $p < 0.001$ level. The Δ (2.17) is more than 2 SD units and reflects heavy exposure to OP compounds. Slightly more than 70% of the exposed workers would be expected to have PChE values below the 2.38 IU/ml lower limit of normal determined by the unexposed controls. Symptomatically, 52 (69%) of the workers reported effects—e.g., loss of appetite, nausea, headache, giddiness, vertigo, fatigue, anorexia, muscular cramps, stomatitits, and watering of the eyes—commonly associated with OP intoxication.

[9] Bogden et al. (1975) compared PChE values in 12 migrant workers exposed to OPs with values found in two unexposed medical-

school personnel. The difference between the means was statistically significant at the $p < 0.01$ level, as shown in Table 1. The Δ (2.60) is more than 2½ SD units and reflects heavy OP exposure. Amost 83% of the migrant workers would be expected to have PChE values below the 5.50 IU/ml lower limit of normal determined by the unexposed controls. Although preexposure data were not available and the number of exposed workers and controls was small, the authors suggested that the evidence indicated an association between health symptoms—e.g., frequent headaches, blurred vision, dizziness, and muscle weakness—reported by the workers, and pesticide exposure.

[10] Knaak et al. (1978) compared PChE values in the blood of 79 male vineyard workers complaining of cholinergic symptoms following exposure to OP compounds during reentry with those of Sacramento Blood Bank controls. The PChE activity for the workers was found to be significantly ($p < 0.001$) depressed below control values. The Δ (4.07) is more than 4 SD units and reflects very heavy OP exposure. More than 99% of the exposed grape pickers would be expected to have PChE values below the 7.01 μmol/min · ml lower limit of normal determined by unexposed controls.

As shown in Table 1, the difference in the mean PChE value between the OP exposed and control groups is statistically significantly depressed in 9 of the 10 (90%) comparison populations, while it is clear from the analyses presented that the severity of exposure ranges from the no effect level to symptomatic conditions. For example, the p value for the occupationally exposed workers studied by [1] Warnick and Carter (1972) and for the migrant workers studied by [9] Bogden et al. (1975) are identical ($p < 0.01$), yet the farmers group was asymptomatic, while 100% of the migrant group reportedly experienced cholinergic symptoms, e.g., headaches, blurred vision, dizziness, and general weakness. The large difference of more than 2 SD units in the value of Δ (2.60) for Bogden et al. (1975) and the value of Δ (0.24) for Warnick and Carter (1972) suggests heavy exposure among the migrants. Using the Z statistic, it was estimated that 83% of the migrant workers would be expected to have PChE values below the lower limit of normal for the controls.

The high percentage of migrants expected to fall below normal values for PChE raises the question of the correlation between the percentage of workers experiencing symptoms with the percentage of workers falling below the lower limit of normal value. This question would be expected to be of concern to physicans and others responsible for the health care of workers with OP exposure. In exploring this relationship it must be considered that any estimate of the degree of ChE inhibition associated with a toxic reaction is provisional, although it has been suggested that depression that exceeds 25% of the normal value for PChE and 50% for RBChE constitutes occupational poisoning

(Vanderkar, 1980). Therefore, Δ and the estimate of the percentage of workers expected to have PChE values below the lower limit of normal should be expected to do no more than correlate closely with the percentage of workers experiencing symptoms, thereby being somewhat predictive of the numbers of ill workers expected as a result of the exposure incident. For example, [8] Bhatnagar et al. (1982) reported that 69% of the factory workers studied were symptomatic, while the Δ was independently estimated to have a value of 2.17 (indicating heavy exposure), with slightly more than 70% of the workers expected to have PChE values below the lower limit of normal for the controls. In another example, [10] Knaak et al. (1978) reported that as many as 98% of grape pickers exposed to Torak (dialifor) and Zolone (phosalone) experienced cholinergic symptoms, and independently, Δ was estimated to have a value of 4.07 (indicating very heavy exposure), with more than 99% of the grape pickers expected to have PChE values below the lower limit of normal for the controls.

Utilizing those studies for which the percent of exposed subjects showing symptoms could be estimated ([1], [4], [8], [9], and [10]), a regression analysis was performed using Δ as the predictor variable. The predicted percent of subjects showing symptoms is given by

$$\% \text{ With symptoms} = 1.2 \times (\% \text{ below normal}) - 16$$

The two estimates are significantly correlated, $r = 0.98$ $p < 0.01$. This would appear to lend validity to the use of the standardized unit of measurement as an indicator of OP exposure.

It seems clear that the standardized unit of measurement Δ effectively denotes exposure to OPs among workers and provides a dimension-free measurement of PChE depression that permits comparison, based on summary statistics, among studies utilizing various methods, units of measurement, and different sample sizes. There is no reason to believe that this approach would not work just as effectively in comparing studies measuring RBChE values; however, as previously discussed, since PChE is reportedly more sensitive to OP exposure and may provide the best early warning of excessive exposure, we elected to use PChE in the development of Δ.

Since we were unable to identify studies where different analytical methods were used on the same population to determine RBChE or PChE values, it was not possible to form a judgement as to either the stability of Δ or the percentage of workers expected to fall below the lower limits of normal for controls. However, since we have developed a dimension-free standardized deviation unit of measurement, independent of sample size and assay method, there is little reason to believe that values would differ, regardless of the analytical method employed.

One might also question the quality of the studies used in the ex-

amples, i.e., the selection of controls, the lack of preexposure values for determining ChE depression, the size of the population under study, and the limited exposure history. Although the reported studies may have their shortcomings, the dimensionless unit of measurement Δ is a mathematically derived quantity, independent of the data source, and has been applied in this instance to studies reported in peer-reviewed journals.

In summary, the use of the Δ value to estimate the number of workers expected to fall below the lower limit of normal PChE values essentially provides a common reference, regardless of the unit of measurement, for comparison purposes, and permits a judgement to be made on the findings of various studies concerned with the severity of pesticide exposure.

REFERENCES

Bhatnagar, V. K., Saigal, S., Singh, S. P., Khemani, L. D., and Malviya, A. N. 1982. Survey amongst workers in pesticide factories. *Toxicol Lett.* 10:129–132.

Bogden, J. D., Quinones, M. A., and Nakah, A. E. 1975. Pesticide exposure among migrant workers in southern New Jersey. *Bull. Environ. Contam. Toxicol.* 13:513–517.

Bogusz, M. 1968. Influence of insecticides on the activity of some enzymes contained in human serum. *Clin. Chem. Acta.* 19:367–369.

Burns, J. E., and Parker, R. D. 1975. An investigation of the safety of cotton reentry after organophosphate application. *Arch. Environ. Contam. Toxicol.* 3:344–351.

Callaway, S., Davies, D. R., and Rutland, J. P. 1951. Blood cholinesterase levels and range of personal variation in a healthy adult population. *Br. Med. J.* 2:812.

Duncan, R. C., and Griffith, J. 1985. A monitoring study of urinary metabolites and selected symptomatology among Florida citrus workers. *J. Toxicol. Environ. Health* 16:509–521.

Durham, W. F., and Hayes, W. J., Jr. 1962. Organic phosphorus poisoning and its therapy. *Arch. Environ. Health* 5:21–47.

Freedman, A. M., Willis, A., and Himwich, H. E. 1949. Correlation between signs of toxicity and poisoning. *Am. J. Physiol.* 157:80.

Gage, J. C. 1967. The significance of blood cholinesterase activity measurements. *Residue Rev.* 18:159.

Griffith, J., and Duncan, R. C. 1985. Alkyl phosphate residue values in the urine of Florida citrus fieldworkers compared to the National Health and Nutrition Study (HANES) sample. *Bull. Environ. Contam. Toxicol.* 34:210–215.

Grob, D., and Harvey, A. M. 1949. Observations on the effects of tetraethyl pyrophosphate (TEPP) in man, and on its use in the treatment of myasthenia gravis. *Johns Hopkins Hosp. Bull.* 84:532.

Hayes, W. J., Jr., Dixon, E. M., Batchelor, G. S., and Upholt, W. M. 1957. Exposure to organic phosphorous sprays and occurrence of selected symptoms. *Public Health Rep.* 72:787–794.

Knaak, J. B., Peoples, S. A., Jackson, T. J., Fredrickson, A. S., Enos, R., Maddy, K. T., Bailey, J. B., Dusch, M. E., Gunther, F. A., and Winterlin, W. L. 1978. Reentry problems involving the use of dialifor on grapes in the San Joaquin valley of California. *Arch. Environm. Contam. Toxicol.* 7:465–481.

Kraus, J. F., Mull, R., Kurtz, P., Winterlin, W., Franti, C. E., Borhani, N., and Kilgore, W. 1981. Epidemiologic study of physiological effects in usual and volunteer citrus workers from organophosphate pesticide residues at reentry. *J. Toxicol. Environ. Health* 8:169–184.

Levin, H. S., Rodnitzky, R. L., and Mick, D. L. 1976. Anxiety associated with exposure to organophosphate compounds. *Arch. Gen. Psychiatry.* 33:225–228.

Milby, T. H., Ottoboni, F., and Mitchell, H. W. 1964. Parathion residue poisoning among orchard workers. *J. Am. Med. Assoc.* 189:351–356.

Popendorf, W. P., Spear, R. C., Leffingwell, J. T., Yager, J., and Kahn, E. 1979. Harvester exposure to zolone (phosalone) residues in peach orchards. *J. Occup. Med.* 21:189–194.

Rider, J. A., Moeller, H. C., Puletti, E. J., and Swader, J. I. 1969. Toxicity of parathion, systox, octamethyl-pryophosphoramide, and methyl parathion in man. *Toxicol. Appl. Pharmacol.* 14:603–611.

Rodnitzky, R. L., Levin, H. S., and Mick, D. L. 1975. Occupational exposure to organophosphate pesticides. *Arch. Environ. Health* 30:98–103.

Simmons, S. W. 1968. The pesticides program activities of the public health service. *Public Health Rep.* 83:967–974.

Tabershaw, I. R., and Cooper, M. D. 1966. Sequelae of actue organic phosphate poisoning. *J. Occup. Med.* 8:5–20.

Tocci, P. M., Mann, J. B., Davies, J. E., and Edmundson, W. F. 1969. Biochemical differences found in persons chronically exposed to high levels of pesticides. *Ind. Med.* 38:40–47.

Vandekar, M. 1980. Minimizing occupational exposure to pesticides: Cholinesterase determination and organophosphate poisoning. *Residue Rev.* 75:67–80.

Ware, G. W., Morgan, D. P., Estesen, B. J., and Cahill, W. P. 1975. Establishment of reentry intervals for organophosphate-treated cotton fields based on human data: III. 12 To 72 hours post-treatment exposure to monocrotophos, ethyl- and -methyl parathion. *Arch. Environ. Contam. Toxicol.* 3:289–306.

Warnick, S. L., and Carter, J. E. 1972. Some findings in a study of workers occupationally exposed to pesticides. *Arch. Environ. Health* 25:265–270.

Wicker, G. W., Williams W. A., and Gutherie, F. E. 1979. Exposure of fieldworkers to organophosphorous insecticides: Sweet corn and peaches. *Arch. Environ. Contam. Toxicol.* 8:175–182.

Wolfsie, J. H., and Winter, G. D. 1952. Statistical analysis of normal human red blood cell and plasma cholinesterase activity values. *A.M.A. Arch. Ind. Hyg.* 6:43–49.

Zavon, M. R. 1965. Blood cholinesterase levels in organic phosphate intoxication. *J.A.M.A.* 192:51–52.

Received July 3, 1985
Accepted December 3, 1985

This article documents research that was conducted under the auspices of the U.S. Environmental Protection Agency (USEPA). As an arm of the government, the USEPA has a paid up, non-exclusive, irrevocable, worldwide license to reproduce, prepare derivative works, and distribute to the public all of the material contained herein, and to grant others acting on its behalf the right to do so. The USEPA grants to the National Technical Information Service, Department of Commerce, the right to act as its agent in the distribution of this material.